WEST Search History

DATE: Thursday, July 31, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,DWPI; PLUR=YES; OP=ADJ			
L7	L6 same (ligand or fasl or apo-2L or apo2-l or apo2l)	265	L7
L6	tnfr-6$ or dcr3 or tr4 or ztnfr-5 or ntr-1 or opg-2 or flint1 or flint!1 or hapo6 or apo6	3132	L6
L5	(L3.ti. or l3.ab.) and (fasL or fas-l or apo2 or apo-2 or light)	34	L5
L4	L3 and (fasL or fas-l or apo2 or apo-2 or light)	1254	L4
L3	tnfr-6? or dcr3 or tr4 or ztnfr-5 or ntr-1 or opg-2 or flint1 or flint!1 or hapo6 or apo6	3130	L3
DB=DWPI; PLUR=YES; OP=ADJ			
L2	L1 and (fasL or fas-l or apo-2 or apo2)	0	L2
L1	9946376	2	L1

END OF SEARCH HISTORY

WEST

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L7: Entry 258 of 265 File: DWPI May 22, 2003

DERWENT-ACC-NO: 2003-449572
DERWENT-WEEK: 200342

TITLE: Novel antibody against TNF-related apoptosis inducing ligand, useful for preventing, treating and ameliorating cancers and other hyperproliferative disorders, binds immunospecifically to TRAIL receptor 4 polypeptide

INVENTOR: ROSCHKE, V; ROSEN, C A ; RUBEN, S M ; SALCEDO, T

PATENT-ASSIGNEE: HUMAN GENOME SCI INC (HUMAN)

PRIORITY-DATA: 2002US-403376P (August 15, 2002), 2001US-331309P (November 14, 2001), 2002US-377973P (May 7, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2003042367 A2	May 22, 2003	E	405	C12N000/00

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO2003042367A2	November 13, 2002	2002WO-US36431	

INT-CL (IPC): C12 N 0/00

ABSTRACTED-PUB-NO: WO2003042367A
BASIC-ABSTRACT:

NOVELTY - An isolated anti-TRAIL (TNF-related apoptosis- inducing ligand) antibody (I) that immunospecifically binds TRAIL receptor 1 (TR4), comprising a first amino acid sequence having at least 90, preferably 95% identity to a second amino acid sequence selected from VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 or VLCDR3, is new.

DETAILED DESCRIPTION - (I) immunospecifically binds TR4, and comprises a first amino acid sequence having at least 90, preferably 95% identity to a second amino acid sequence selected from VHCDR1 (comprising a sequence of 120 amino acids), VHCDR2 (comprising a sequence of 128 amino acids), VHCDR3 (comprising a sequence of 128 amino acids), VLCDR1 (comprising a sequence of 111 amino acids), VLCDR2 (comprising a sequence of 108 amino acids) or VLCDR3 (comprising a sequence of 109 amino acids). All the sequences are fully defined in the specification.

INDEPENDENT CLAIMS are also included for:

(1) an antibody that competitively inhibits the binding of (I) to TR4;

(2) an isolated cell that produces (I);

(3) an antibody that binds the same epitope one TR4 polypeptide as (I);

(4) treating, preventing or ameliorating a cancer, by administering (I) or a composition comprising (I);

(5) inhibiting the growth of or killing TR4- expressing cells, by administering (I) or a composition comprising (I) to the cell;

(6) a kit comprising (I);

(7) a hybridoma cell line selected from hybridoma cell lines contained in ATCC deposit numbers PTA-3149, PTA-2687, PTA-3369, PTA-2730, PTA-2729, PTA-2728, PTA-3368 and PTA-2731; and

(8) inducing apoptosis of cells that express TR4 and TRAIL receptor 2 (TR7), by contacting the cells with a first antibody that specifically binds TR4 and a second antibody that specifically binds TR7.

ACTIVITY - Cytostatic; Antiparkinsonian; Nootropic; Neuroprotective; Anticonvulsant; Immunosuppressive; Antirheumatic; Antiarthritic; Antiasthmatic; Antiallergic; Virucide; Antiinflammatory; Anti-HIV; Antianemic; Vasotropic; Antibacterial; Immunomodulator; Metabolic; Cytostatic; Cerebroprotective; Ophthalmological; Antidiabetic; Antiulcer; Antipsoriatic; Vulnerary.

MECHANISM OF ACTION - Diminishes or abolishes the ability of TRAIL to bind TR4; Agonist or antagonist of TR4 receptor; Stimulates apoptosis of TR4 expressing cells; Upregulates or downregulates TRAIL receptor expression (claimed); Vaccine; Angiogenesis promoter.

Anti-TRAIL receptor antibodies were tested for their ability to induce apoptosis of TRAIL receptor expressing cells, alone or in combination with chemotherapeutic or cross-linking agents. Briefly, hybridoma supernatants were tested for activity to induce TRAIL receptor mediated apoptosis of TR4 expressing cell lines, SW480 and HeLa. HT1080 fibrosarcoma cell line, which failed to express TR4, was used as a negative control. To induce apoptosis, either HeLa or SW480 cells were incubated with monoclonal antibodies (e.g. 7.3 or 7.12) or a human IgG2 a control antibody. One day prior to assay, cells (0.3 multiply 106 cells/ml) were seeded into wells of a 96-well plate and allowed to adhere overnight. The following day, the test antibody was added either in the presence or absence of 2.0 micrograms/ml cycloheximide. The potency of anti-TRAIL receptor monoclonal antibody was compared to recombinant human (rhu)TRAIL-FLAG protein. Recombinant human TRAIL was used in the presence of anti-FLAG enhancer antibody at 2 mu g/ml. The effect of secondary crosslinking was also assessed by measuring the ability of the monoclonal antibodies 7.3 or 7.12 to kill cells alone, or in the presence of a secondary goat-anti-human Ig Fc specific antibody. The secondary crosslinking antibody was added to cells at an equivalent concentration as the test monoclonal antibody. The ability of a chemotherapeutic agent to sensitize cells to killing through the monoclonal antibody 7.12 in the presence of Topotecan. The results showed that monoclonal antibodies 7.3 and 7.12 reduced cell viability to 50% of the control. Further, monoclonal antibodies 7.3 and 7.12 were able to kill cells equally well in the presence or absence of secondary crosslinking reagents.

USE - (I) is useful for treating, preventing or ameliorating cancer (e.g. cancers of colon, breast, uterine, pancreas, lung and gastrointestine, and Kaposi's sarcoma), and for inhibiting the growth of or killing TR4 expressing cells. (I) is administered in combination with a chemotherapeutic agent e.g. irinotecan, paclitaxel (TAXOL) and gemcitabine, TRAIL or a cross-linking agent. (I) is also useful for detecting the expression of a TR4 polypeptide, by assaying the expression of TR4 polypeptide in a biological sample of an individual using (I), and comparing the level of TR4 polypeptide with a standard level of TRAIL receptor polypeptide. (I) is also useful for detecting, diagnosing, prognosing and monitoring cancers and other hyperproliferative disorders, by assaying the expression of TR4 polypeptide in a biological sample of an individual using (I), and comparing the level of TR4 polypeptide with a standard level of TR4 polypeptide (claimed). (I) is also useful for treating, preventing and ameliorating neurodegenerative disorders (e.g. Parkinson's disease, Alzheimer's disease and Huntington's disease), autoimmune disorders (e.g. lupus, rheumatoid arthritis, multiple sclerosis, myasthenia gravis, Hashimoto's disease and immunodeficiency syndrome), inflammatory disorders (e.g. asthma, allergic disorders and rheumatoid arthritis), infectious diseases (e.g. AIDS, herpes viral infections and other viral infections), myelodysplastic syndromes (e.g. aplastic anemia), graft-versus- host disease, ischemic injury, liver injury, toxin-induced liver disease, septic shock, cachexia and anorexia, and proliferative disorders. (I) is also useful for treating

cardiovascular disorders, cerebrovascular disorders, thrombotic microangiopathies, ocular disorders associated with neovascularization, diabetes, ulcerative colitis and psoriasis, and for wound healing. (I) is also useful as a diagnostic tool to monitor the expression of TRAIL receptor expression on cells, for purifying, detecting and targeting polypeptides, for immunophenotyping of cell lines and biological samples, and for identifying epitopes of TRAIL polypeptide.

ADVANTAGE - (I) stimulates apoptosis of TR4 expressing cells better than an equal concentration of TRAIL polypeptide stimulates apoptosis of TR4 expressing cells. (I) stimulates apoptosis of TR4 expressing cells equally well in the presence or absence of antibody cross-linking reagents (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the flow cytometric staining of HeLa, SW480 and HT1080 cells for TR4 expression using monoclonal antibody 7.3.

ABSTRACTED-PUB-NO: WO2003042367A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.1/9

DERWENT-CLASS: B04 D16 K08
CPI-CODES: B04-F0100E; B04-F05; B04-G01; B11-C07A4; B11-C09; B14-A02; B14-C09B; B14-E10C; B14-E11; B14-F01; B14-F02; B14-F02D; B14-F02F2; B14-F03; B14-F04; B14-G01B; B14-G02A; B14-G02C; B14-H01; B14-J01A3; B14-J01A4; B14-K01A; B14-L06; B14-N03; B14-N11; B14-N12; B14-N17; B14-N17B; B14-N17C; B14-S01; B14-S04; B14-S06; D05-H09; D05-H10; D05-H11; D05-H14; D05-H15; K08-X; K09-B;

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L7: Entry 259 of 265 File: DWPI Oct 10, 2002

DERWENT-ACC-NO: 2003-040669
DERWENT-WEEK: 200303

TITLE: Novel antibody for treating, or preventing disease or disorder, comprises amino acid sequence having identity to other amino acid sequence of either variable heavy/light chain-complementarity determining regions

INVENTOR: ROSCHKE, V; ROSEN, C A ; RUBEN, S M ; SALCEDO, T

PATENT-ASSIGNEE: HUMAN GENOME SCI INC (HUMAN)

PRIORITY-DATA: 2001US-327359P (October 9, 2001), 2000US-246612P (November 8, 2000), 2000US-248847P (November 16, 2000), 2000US-252904P (November 27, 2000), 2001US-295018P (June 4, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200279377 A2	October 10, 2002	E	375	C12N000/00

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 200279377A2	November 7, 2001	2001WO-US42996	

INT-CL (IPC): C12 N 0/00

ABSTRACTED-PUB-NO: WO 200279377A
BASIC-ABSTRACT:

NOVELTY - An isolated antibody (I) comprising a first amino acid sequence having 95 % identity to a second amino acid sequence of either variable heavy chain or light chain-complementarity determining regions (VHCDR1)/VLCDR1, VHCDR2/VLCDR2 or VHCDR3/VLCDR3 having a 120 or 128 (S1), or 111, 108 or 109 (S2) residue amino acid sequence, respectively, is new. S1 and S2 are given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated antibody (II) comprising an amino acid sequence that is at least 90 % identical to VH or VL domain of any one of S1 or S2 respectively, or both, where the antibody immunospecifically binds to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) receptor 1 (TRAIL-R1) (referred as TR4);

(2) an isolated cell (III) that produces (I);

(3) an antibody (IV) that binds the same epitope on a TR4 polypeptide as (I);

(4) detecting (M1) expression of a TR4 polypeptide, or detecting, diagnosing, prognosing or monitoring cancers, and other hyperproliferative disorders, comprising:

(a) assaying the expression of a TR4 polypeptide in a biological sample from an individual using (I); and

(b) comparing the level of a TR4 polypeptide with a standard level of a tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) receptor polypeptide (e.g. the level in normal biological samples);

(5) a kit (V) comprising (I);

(6) a hybridoma cell line (VI) selected from the hybridoma cell lines contained in ATCC Deposit No. PTA-3149, PTA-2687, PTA-3369, PTA-2730, PTA-2729, PTA-2728, PTA-3368, and PTA-2731; and

(7) an antibody (VII) expressed by (VI).

ACTIVITY - Cytostatic; Anti-HIV; Immunosuppressive; Neuroprotective; Antiinflammatory; Vasotropic; Dermatological; Antirheumatic; Antiarthritic; Antipsoriatic; Vulnerary.

MECHANISM OF ACTION - Antibody therapy; Agonist or antagonist of TRAIL; Inhibitor of the growth of TR4 expressing cells; Modulator of apoptosis; Regulator of TRAIL receptor expression; Inhibitor of TRAIL binding to TR4.

Anti-TRAIL receptor antibodies were tested for their ability to induce apoptosis of TRAIL receptor expressing cells, alone or in combination with chemotherapeutic or cross-linking agents. Hybridoma supernatants were tested for activity to induce TRAIL receptor mediated apoptosis of TR4 expressing cell lines, SW480 and HeLa. HT1080 fibrosarcoma cell line, which failed to express TR4, was used as a negative control. To induce apoptosis, either HeLa or SW480 cells were incubated with the indicated concentration of monoclonal antibodies or a human IgG2a control antibody. One day prior to assay, cells were seeded into wells of a 96-well plate and allowed to adhere overnight. The following day, the test antibody was added either in the presence or absence of cycloheximide. The effect of secondary crosslinking was also assessed by measuring the ability of the monoclonal antibodies 7.3 or 7.12 to kill cells alone, or in the presence of a secondary goat-anti-human IgFc specific antibody. The secondary crosslinking antibody was added to cells. The ability of a chemotherapeutic agent to sensitize cells to killing by the monoclonal antibody 7.12, was assessed by treating either Hela or SW480 cells with monoclonal antibody 7.12 in the presence of Topotecan. This showed that monoclonal antibodies 7.3 and 7.12 were able to kill cells equally well in the presence or absence of secondary cross linking reagents. Thus, these showed that antibody 7.12 administered with particular chemotherapeutic drugs (e.g. cycloheximide and topotecan) was able to kill TRAIL receptor expressing cells in a synergistic manner.

USE - (I) is useful for treating, preventing or ameliorating a disease or disorder, by administering (I) or a composition containing (I) to an animal (human). The disease or disorder is associated with increased or decreased apoptosis, cancer (such as colon, breast, uterine, pancreatic, lung, gastrointestinal, and Kaposi's sarcoma), graft versus. host disease (GVHD), infectious disease, acquired immunodeficiency syndrome (AIDS), or neurodegenerative disorder. (I) is administered in combination with a chemotherapeutic agent selected from irinotecan, paclitaxel (TAXOL (RTM), and gemcitabine. (I) is useful for treating a disease or disorder associated with aberrant TRAIL receptor expression, lack of TRAIL receptor function, aberrant TRAIL expression, or lack of TRAIL function, by administering (I) or a composition of (I) to an animal. (I) is useful for inhibiting the growth of or killing TR4 expressing cells, by administering to an animal in which such inhibition of growth or killing of TR4 receptor expressing cells is desired, (I) or a composition containing (I) in an amount effective to inhibit the growth of or kill TR4 expressing cells. (All claimed). (I) is useful as a diagnostic tool to monitor the expression of TRAIL receptor expression on cells. (I) is useful to detect, purify, and target the polypeptides, and in immunoassays for qualitatively and quantitatively measuring levels of TRAIL receptor polypeptides in a sample. (I) is useful for immunophenotyping of cell lines and biological samples. (I) is useful to identify epitopes of a human TRAIL receptor polypeptides. The identified epitopes of (I) is useful as vaccine to immunize an individual to elicit antibodies against the naturally occurring forms of TRAIL receptor polypeptides. (I) is useful for treating diseases and/or disorders such as autoimmune disorders like multiple sclerosis, Behcet's disease, lupus erythematosus. (I) is also useful for treating inflammatory diseases such as rheumatoid arthritis, and psoriasis, cardiovascular disorders, in promoting angiogenesis, wound healing, in regulating immune response.

ABSTRACTED-PUB-NO: WO 200279377A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/9

DERWENT-CLASS: B04 C06 D16
CPI-CODES: B04-B03A; B04-F05; B04-G01; B05-A04; B06-A03; B06-E05; B06-F03; B11-C07A; B12-K04A1; B14-A01; B14-A02B1; B14-C06; B14-C09B; B14-F01; B14-F02; B14-G01B; B14-G02C; B14-H01; B14-H01B; B14-J01; B14-N17C; B14-S01; C04-F05; C04-G01; C05-A04; C06-F03; C11-C07A; C12-K04A1; C14-A01; C14-A02B1; C14-C06; C14-C09B; C14-F01; C14-F02; C14-G01B; C14-G02C; C14-H01; C14-H01B; C14-J01; C14-N17C; C14-S01; D05-H11A1; D05-H15;

DE Human tumour necrosis factor receptor-6 alpha protein.
XX
KW Human tumour necrosis factor receptor-6 alpha; TNFR-6 alpha; TNFR-6 beta;
KW endothelial cells; keratinocytes; normal prostate; apoptosis;
KW prostate tumour tissue.
OS Homo sapiens.
FH Key Location/Qualifiers
FT Peptide 1..30
FT Protein 31..300
FT /note= "TNFR-6 alpha"
FT Region 31..282
FT /note= "Soluble extracellular domain"

PN WO9830694-A2.
PD 16-JUL-1998.
PF 13-JAN-1998; 98WO-US00153.
XX
PR 14-JAN-1997; 97US-0035496.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Ebner R, Feng P, Gentz RL, Ni J, Ruben SM, Yu G;
XX
DR WPI; 1998-399142/34.
DR N-PSDB; V39085.
XX
PT Human tumour necrosis factor receptors 6-alpha and 6-beta - used in
PT the diagnosis of immune system-related disorder(s)
XX
PS Claim 20; Fig 1; 91pp; English.
XX
CC The present sequence represents the human tumour necrosis factor
CC receptor-6 alpha (TNFR-6 alpha) protein. The invention also provides
CC for the TNFR-6 beta protein (W63623). TNFR-6 alpha and TNFR-6 beta are
CC members of the tumour necrosis factor receptor (TNFR) family. TNFRs
CC are expressed in endothelial cells, keratinocytes, normal prostate and
CC prostate tumour tissue. For a number of disorders of these cells,
CC particularly of the immune system, substantially altered (whether
CC increased or decreased) levels of TNFR-6 alpha and/or TNFR-6 beta gene
CC expression can be detected, therefore the TNFR-6 alpha and TNFR-6 beta
CC polypeptides, nucleic acids and antibodies are claimed to be useful in
CC the diagnosis of such disorders. Mutations of the TNFR-6 alpha and
CC TNFR-6 beta genes can also be detected. The TNFR polypeptides are
CC also claimed to be useful for identifying ligands which may be useful
CC in the treatment of apoptosis related disorders.
XX
SQ Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 19; Length 300;
Best Local Similarity 100.0%; Pred. No. 3.8e-122;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MRALEGPGLSLLCLVLALPALLPVPAVRGVAETPTYPWRDAETGERLVCAQCPPGTFVQR 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 1 mralegpglsllclvlalpallpvpavrgvaetptypwrdaetgerlvcaqcppgtfvqr 60

```
Qy      61 PCRRDSPTTCGPCPPRHYTQFWNYLERCRYCNVLCGEREEEARACHATHNRACRCRTGFF 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 pcrrdspttcgpcpprhytqfwnylercrycnvlcgereeearachathnracrcrtgff 120

Qy     121 AHAGFCLEHASCPPGAGVIAPGTPSQNTQCQPCPPGTFSASSSSSEQCQPHRNCTALGLA 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 ahagfclehascppgagviapgtpsqntqcqpcppgtfsassssseqcqphrnctalgla 180

Qy     181 LNVPGSSSHDTLCTSCTGFPLSTRVPGAEECERAVIDFVAFQDISIKRLQRLLQALEAPE 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 lnvpgssshdtlctsctgfplstrvpgaeeceravidfvafqdisikrlqrllqaleape 240

Qy     241 GWGPTPRAGRAALQLKLRRRLTELLGAQDGALLVRLLQALRVARMPGLERSVRERFLPVH 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 gwgptpragraalqlklrrrltellgaqdgallvrllqalrvarmpglersvrerflpvh 300
```

DE Human FLINT #2 protein sequence.
XX
KW Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL;
KW apoptosis; inflammation; cancer; diabetes; acute liver failure;
KW sepsis; hepatitis; ischaemia-associated injury; hypercoagulation;
KW reperfusion-associated injury; aplastic anaemia; differentiation;
KW growth; myelodysplastic syndrome; pancytopenic condition;
KW myocardial ischaemia.
XX
OS Homo sapiens.
XX
PN WO9950413-A2.
XX
PD 07-OCT-1999.
XX
PF 30-MAR-1999; 99WO-US06797.
XX
PR 30-MAR-1998; 98US-0079856.
PR 20-MAY-1998; 98US-0086074.
PR 09-SEP-1998; 98US-0099643.
PR 17-DEC-1998; 98US-0112577.
PR 18-DEC-1998; 98US-0112703.
PR 18-DEC-1998; 98US-0112933.
PR 22-DEC-1998; 98US-0113407.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Bumol TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JG;
PI Hui KY, Kharitonenkov A, Mizrahi J, Na S, Noblitt TW, Reidy CA;
PI Song HY, Wang J, Wu X, Zuckerman SH;
XX
DR WPI; 1999-591319/50.
DR N-PSDB; Z25376.
XX
PT Use of mature FLINT for treating acute liver failure, inflammation,
PT cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic
PT and proinflammatory activity
XX
PS Example 2; Fig 2; 99pp; English.
XX
CC The present invention describes therapeutic applications of mature FLINT
CC (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
CC (mFLINT), which is a member of the tumour necrosis factor receptor
CC superfamily, is used for treating acute liver failure, inflammation of
CC the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
CC with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
CC injury or disorder such as hypercoagulation (including use with
CC thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
CC or disorder, Type I diabetes, cancer, cell damage or damage to an
CC innocent bystander tissue that is induced by a chemotherapeutic agent or
CC therapeutic irradiation, treating haematopoietic progenitor cells that
CC have been exposed to therapeutic radiation or chemotherapy, aplastic
CC anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
CC also used for promoting the growth or differentiation of a haematopoietic
CC progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
CC resulting from abnormal myocardial ischaemia. The present sequence
CC represents human FLINT.

XX
SQ Sequence 302 AA;

Query Match 98.5%; Score 1610; DB 20; Length 302;
Best Local Similarity 98.7%; Pred. No. 3.1e-120;
Matches 298; Conservative 0; Mismatches 2; Indels 2; Gaps 1;

```
Qy       1 MRALEGPGLSLLCLVLALPALLPVPAVRGVAETPTYPWRDAETGERLVCAQCPPGTFVQR 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mralegpglsllclvlalpallpvpavrgvaetptypwrdaetgerlvcaqcppgtfvqr 60

Qy      61 PCRRDSPTTCGPCPPRHYTQFWNYLERCRYCNVLCGEREEEARACHATHNRA--CRCRTG 118
           |||||||||||||||||||||||||||||||||||||||||||||||||||  ||||||
Db      61 pcrrdspttcgpcpprhytqfwnylercrycnvlcgereeearachathnracrcrcrtg 120

Qy     119 FFAHAGFCLEHASCPPGAGVIAPGTPSQNTQCQPCPPGTFSASSSSSEQCQPHRNCTALG 178
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 ffahagfclehascppgagviapgtpsqntqcqpcppgtfsassssseqcqphrnctalg 180

Qy     179 LALNVPGSSSHDTLCTSCTGFPLSTRVPGAEECERAVIDFVAFQDISIKRLQRLLQALEA 238
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 lalnvpgssshdtlctsctgfplstrvpgaeeceravidfvafqdisikrlqrllqalea 240

Qy     239 PEGWGPTPRAGRAALQLKLRRRLTELLGAQDGALLVRLLQALRVARMPGLERSVRERFLP 298
           |||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 pegwaptpragraalqlklrrrltellgaqdgallvrllqalrvarmpglersvrerflp 300

Qy     299 VH 300
           |
Db     301 wh 302
```

DE A human tumour necrosis factor-R2-like proteins (TR2P)-1.
XX
KW Human tumour necrosis factor-R2-like protein; TR2P; achondroplasia;
KW osteoporosis; developmental disorder; Cushing's syndrome;
KW muscular dystrophy; epilepsy; hereditary neuropathy;
KW Charcot-Marie-Tooth disease; neurofibromatosis; hypothyroidism;
KW hydrocephalus; seizure disorder; cerebral palsy; spinal bifida;
KW congenital glaucoma; cataract; sensorineural hearing loss;
KW reproductive disorder; infertility; ovulatory defect; endometriosis;
KW autoimmune disorder; ectopic pregnancy; teratogenesis; spermatogenesis;
KW immunological disorder; AIDS; Addison's disease; allergy; bronchitis;
KW athersclerosis; diabetes mellitus; Chron's disease; lupus;
KW irritable bowel syndrome; multiple sclerosis; infection;
KW neoplastic disorder; adenocarcinoma; leukaemia; lymphoma; melanoma;
KW myeloma; sarcoma.
XX
OS Homo sapiens.
XX
PN WO9931128-A2.
XX
PD 24-JUN-1999.
XX
PF 02-DEC-1998; 98WO-US25649.
XX
PR 16-DEC-1997; 97US-0991945.
XX
PA (INCY-) INCYTE PHARM INC.
XX
PI Au-Young J, Bandman O, Hillman JL, Kaser MR, Tang YT;
XX
DR WPI; 1999-457916/38.
DR N-PSDB; X89503.
XX
PT New tumour necrosis factor-R2-like protein - useful in the treatment
PT of osteogenesis, developmental, reproductive, immunological and
PT neoplastic disorders
XX
PS Claim 1; Fig 1A-C; 81pp; English.
XX
CC The present sequence represents a human tumour necrosis factor-R2-like
CC protein (TR2P). The protein is used to treat and prevent osteogenesis,
CC developmental, reproductive, immunological and neoplastic disorders, and
CC also to diagnose disorders associated with TR2 protein expression. Such
CC disorders include osteogenesis disorders such as achondroplasia and
CC osteoporosis, developmental disorders such as Cushing's syndrome,
CC muscular dystrophy, and epilepsy, hereditary neuropathies such as
CC Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism,
CC hydrocephalus, seizure disorders such as cerebral palsy and spinal
CC bifida, congenital glaucoma, cataract, or sensorineural hearing loss,
CC reproductive disorders such as infertility, ovulatory defects and
CC endometriosis, autoimmune disorders, ectopic pregnancy and teratogenesis,
CC disruption of spermatogenesis, immunological disorders such as AIDS,
CC Addison's disease, allergies, bronchitis, athersclerosis, diabetes
CC mellitus, Chron's disease, lupus and irritable bowel syndrome, multiple
CC sclerosis, viral, fungal, helminthic, parasitic and protozoal infections,
CC and neoplastic disorders including adenocarcinoma, leukaemia, lymphoma,
CC melanoma, myeloma, sarcoma, and teratocarcinoma.

XX
SQ Sequence 245 AA;

Query Match 83.4%; Score 1362; DB 20; Length 245;
Best Local Similarity 99.6%; Pred. No. 1.1e-100;
Matches 244; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Qy       1 MRALEGPGLSLLCLVLALPALLPVPAVRGVAETPTYPWRDAETGERLVCAQCPPGTFVQR 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mralegpglsllclvlalpallpvpavrgvaetptypwrdaetgerlvcaqcppgtfvqr 60

Qy      61 PCRRDSPTTCGPCPPRHYTQFWNYLERCRYCNVLCGEREEEARACHATHNRACRCRTGFF 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 pcrrdspttcgpcpprhytqfwnylercrycnvlcgereeearachathnracrcrtgff 120

Qy     121 AHAGFCLEHASCPPGAGVIAPGTPSQNTQCQPCPPGTFSASSSSSEQCQPHRNCTALGLA 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 ahagfclehascppgagviapgtpsqntqcqpcppgtfsassssseqcqphrnctalgla 180

Qy     181 LNVPGSSSHDTLCTSCTGFPLSTRVPGAEECERAVIDFVAFQDISIKRLQRLLQALEAPE 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 lnvpgssshdtlctsctgfplstrvpgaeeceravidfvafqdisikrlqrllqaleape 240

Qy     241 GWGPT 245
            ||||
Db     241 dwgpt 245
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DE Human hAPO6 protein.
XX
KW Tumour necrosis factor receptor; signal transducer molecule; TNF; APO4;
KW developmental abnormality; gestational abnormalitity; prostate cancer;
KW APO6; APO8; APO9; TNRL-1; TNRL-3; diagnosis; treatment; therapy; disease;
KW cytoplasmic domain; immunogen; antibody preparation; breast carcinoma;
KW apoptosis; human.
XX
OS Homo sapiens.
XX
PN WO9911791-A2.
XX
PD 11-MAR-1999.
XX
PF 04-SEP-1998; 98WO-US18393.
XX
PR 05-SEP-1997; 97US-0924634.
XX
PA (UNIW) UNIV WASHINGTON.
XX
PI Chaudhary PM;
XX
DR WPI; 1999-205191/17.
DR N-PSDB; X23419.
XX
PT New Tumor Necrosis Factor family receptor polypeptides and ligands -
PT useful for diagnosis and treatment of prostate cancer and
PT developmental or gestational abnormalities
XX
PS Claim 29; Fig 9; 156pp; English.
XX
CC This invention describes isolated Tumor Necrosis Factor (TNF) family
CC receptor polypeptides: APO4, APO6, APO8 and APO9 or their active
CC fragments, and isolated TNF related ligands 1 and 3 (TNRL1 and TNRL3) or
CC their active fragments. APO4 is useful for diagnosing prostate cancer
CC by determining levels of APO4 in an individual. Prostate cancer can also
CC be treated using APO4 selective binding agents linked to a therapeutic
CC moiety. APO4 polypeptides are also useful for identifying selective
CC binding agents, useful in diagnosis/treatment of disease by binding of
CC agents to the polypeptide/active fragment which is extracellular, or
CC expressed on the cell surface. The binding is preferably performed in
CC vivo. APO4 polypeptides/ active fragments are also useful for screening
CC for agonists and antagonists by binding and observing the changer in APO4
CC activity. Effective pharmacological agents useful in diagnosis or
CC treatment of disease are also identified using APO4 polypeptides/active
CC fragments and APO4 signal transducer molecules that specifically interact
CC with a cytoplasmic domain of APO4 and detecting a change in level of APO4
CC activity. The method is performed in vivo or in vitro. APO polypeptides
CC are all useful as immunogens for preparing antibodies. APO4 is also
CC useful for diagnosis/treatment of developmental or gestational
CC abnormalities. APO8 was transfected to human breast carcinoma cell line
CC MCF-7, and induced apoptosis.
XX
SQ Sequence 215 AA;

Query Match 70.6%; Score 1153; DB 20; Length 215;

Best Local Similarity 100.0%; Pred. No. 3.3e-84;
Matches 215; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      86 ERCRYCNVLCGEREEEARACHATHNRACRCRTGFFAHAGFCLEHASCPPGAGVIAPGTPS 145
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 ercrycnvlcgereeearachathnracrcrtgffahagfclehascppgagviapgtps 60

Qy     146 QNTQCQPCPPGTFSASSSSSEQCQPHRNCTALGLALNVPGSSSHDTLCTSCTGFPLSTRV 205
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 qntqcqpcppgtfsassssseqcqphrnctalglalnvpgssshdtlctsctgfplstrv 120

Qy     206 PGAEECERAVIDFVAFQDISIKRLQRLLQALEAPEGWGPTPRAGRAALQLKLRRRLTELL 265
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 pgaeeceravidfvafqdisikrlqrllqaleapegwgptpragraalqlklrrrltell 180

Qy     266 GAQDGALLVRLLQALRVARMPGLERSVRERFLPVH 300
           |||||||||||||||||||||||||||||||||||
Db     181 gaqdgallvrllqalrvarmpglersvrerflpvh 215
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